Evolving to Personalized Medicine for Type 2 Diabetes

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KEYWORDS

• Personalized • Precision • Diabetes • Big data • Genomics • Proteomics

KEY POINTS

- Type 2 diabetes is an expensive public health problem that threatens our society at many levels.
- Precision medicine applies not only to medical interventions but also to psychosocial measures, nutrition, and exercise that may also affect individuals differently.
- Using this highly personalized approach, one hopes to achieve better outcomes, more effectively.
- The striking evolution in generating "Big Data," Bio-marker Fingerprints, and the Internet of Things will force all clinicians to be familiar with the terminology and understand the clinical relevance.

To imagine potential future treatment options for type 2 diabetes (T2DM), one must understand past approaches to management. Therapies have been based on traditional herbal therapies to accidental discoveries and more recently based on understanding of the underlying pathophysiology of T2DM. Thus, there is predictable innovation, but we must also be ready to accept disruptive innovation as well. In this brief overview, potential treatments in the near horizon are discussed and also precision medicine approaches and novel disruptive techniques that the clinician needs to be familiar with.

TYPE 2 DIABETES MELLITUS

T2DM accounts for about 85% of the nearly 30 million[1] individuals with diabetes in the United States.[2] Hyperglycemia, the hallmark of diagnosis of diabetes, results after years to decades of dysfunctional physiology of insulin secretion and insulin action. The challenge has been akin to treating a patient with aortic

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regurgitation and heart failure today instead of treating the patient 20 years earlier for aortic stenosis.

Current Treatments

There have been several excellent summaries of evidence-based approaches to using approved medications for T2DM (American Association of Clinical Endocrinologists and American Diabetes Association/European Association for the Study of Diabetes[3]). These statements have evolved to a shared vision of glycemic targets and the need for an individualized approach. The mantra, "the right medication for the right patient at the right time," is still a universal goal of all practitioners.

The management of hyperglycemia is limited by the occurrence of hypoglycemia. Treatment options can be considered as either hypoglycemic or nonhypoglycemic antihyperglycemic therapies. Because euglycemia is an impractical target, we are generally advised to aim for glycemic targets that are safe for the individual.

Customized Approaches to Diabetes Management

Even though the distinction between at least 2 types of diabetes was made centuries ago, the discovery of insulin in 1921 led to a therapy-based differentiation: IDDM, insulin-dependent diabetes mellitus, and NIDDM, non-insulin-dependent diabetes mellitus. In the former, insulin was absolutely critical for maintaining life, whereas, in the latter, lifestyle measures and oral agents may control the hyperglycemia for many years. Of course, the age of onset appeared different, and thus, IDDM was always synonymous with juvenile diabetes and NIDDM was often called adult-onset diabetes mellitus. This distinction led to a variety of clinical approaches.

In the 1980s, the nomenclature was updated to the labels of Type 1 Diabetes Mellitus and Type 2 Diabetes Mellitus, indicating a specific pathophysiology underlying the conditions. This etiologic classification led to active research into immunoregulatory approaches to Type 1 Diabetes Mellitus and clearer recruitment of subjects for clinical research (**Table 1**).

Although this nomenclature has served well for the last 30 years, it was apparent very early on that there are other types of diabetes that do not neatly fit into a predetermined category.

Table 1
Features of type 1 versus type 2 diabetes mellitus

Feature	Type 1	Type 2
Prevalence (%)	0.4	6.6
Annual incidence in United States	15,000	500,000
Ketosis prone	++++	+
Anti-islet cell antibody	+++	–
Anti-GAD antibody	++++	–
Prevalence of other autoimmune conditions	+++	–
Usual age of onset (y)	<30	>40
Prevalence of obesity	+	++++
Family history	+	++++
HLA linkage	DR3, DR4	–
DQ β-polymorphism	++	–